

Clin Orthop Relat Res (2010) 468:2198–2210
DOI 10.1007/s11999-009-1197-8

CLINICAL RESEARCH

Cemented Distal Femoral Endoprostheses for Musculoskeletal Tumor

Improved Survival of Modular versus Custom Implants

Adam J. Schwartz MD, J. Michael Kabo PhD,
Fritz C. Eilber MD, Frederick R. Eilber MD,
Jeffrey J. Eckardt MD

Received: 23 June 2009 / Accepted: 30 November 2009 / Published online: 22 December 2009
© The Author(s) 2009. This article is published with open access at Springerlink.com

Abstract

Background Advocates of newer implant designs cite high rates of aseptic loosening and failure as reasons to abandon traditional cemented endoprosthetic reconstruction of the distal femur.

Questions/purposes We asked whether newer, modular distal femoral components had improved survivorship compared with older, custom-casted designs.

Patients and Methods We retrospectively reviewed 254 patients who underwent distal femoral endoprosthetic reconstruction. We excluded two patients with cementless implants, 27 with expandable prostheses, and 39 who had a nontumor diagnosis. This left 186 patients: 101 with older custom implants and 85 with contemporary modular implants. The minimum followup was 1 month (mean, 96.0 months; range, 1–336 months). The tumor was classified as Stage IIA/IIB in 122 patients, Stage IA/IB or benign in 43, and Stage III or metastatic in 21.

Results Kaplan-Meier analysis revealed overall 10-, 20-, and 25-year implant survival rates of 77%, 58%, and 50%, respectively, using revision of the stemmed components as an end point. The 85 modular components had a greater 15-year survivorship than the 101 custom-designed implants: 93.7% versus 51.7%, respectively. Thirty-five stemmed components (18.8%) were revised for aseptic loosening in 22 patients, implant fatigue fracture in 10, infection in two, and local recurrence in one.

Conclusions Cemented modular rotating-hinge distal femoral endoprostheses demonstrated improved survivorship compared with custom-casted implants during this three-decade experience. Patients with low-grade disease and long-term survivors of high-grade localized disease should expect at least one or more revision procedures in their lifetime.

Level of Evidence Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

This work was performed at University of California Los Angeles Medical Center.

A. J. Schwartz (✉), F. C. Eilber, F. R. Eilber, J. J. Eckardt
Department of Orthopaedic Surgery, University of California
Los Angeles Medical Center, 1250 16th Street Room 745, Santa
Monica, CA 90404, USA
e-mail: adamschwartz2001@yahoo.com

J. M. Kabo
California State University, Northridge, Northridge, CA, USA

Introduction

Before the 1970s, the majority of high-grade musculoskeletal tumors involving the distal femur were treated with transfemoral amputation owing to an unacceptably high rate of recurrence associated with local resection [10, 19, 31, 47]. As effective chemotherapeutic regimens were developed, limb salvage using various techniques gained popularity among orthopaedic oncologists [1, 11, 19, 20, 24, 37, 45, 49, 60, 69]. Today, with effective neoadjuvant chemotherapy, limb salvage is indicated in as much as 90% of patients with musculoskeletal malignancies involving the distal femur [6, 7, 14, 44, 53–55, 57].

Numerous studies document relatively high implant survival after limb salvage for tumors involving the distal

femur [3, 4, 8, 26, 27, 29, 35, 43, 44, 50, 54, 55, 57, 61, 71]. Studies that are available, however, do not stratify patients on the basis of tumor grade, stage of disease, or life expectancy to define the disease-specific survival of implants. This makes it difficult for surgeons to accurately predict how long the implants will last for a given patient population and life expectancy. Additionally, there are limited data available with which to compare implant survival of contemporary modular implant designs with older custom-designed implants no longer in use [8, 44, 48, 70]. Critics of a cemented endoprosthetic reconstruction technique cite rates of aseptic loosening from 8.4% to greater than 30% [2, 30, 38, 63] as the main rationale for abandoning its use in favor of newer designs.

Given the paucity of long-term data concerning cemented distal femoral implants and the heightened interest in alternate fixation designs, we sought to answer the following four questions: (1) Do newer cemented modular implant designs have improved survivorship compared with older custom-designed components? (2) Does tumor grade or stage influence implant survival? (3) What is the typical long-term functional result after a cemented distal femoral replacement? (4) What are the complications associated with this technique?

Patients and Methods

We retrospectively reviewed the electronic and paper charts of all 254 patients who underwent cemented distal femoral endoprosthetic reconstructions for musculoskeletal tumors between December 1980 and December 2008. We excluded 68 patients: 39 patients had distal femoral reconstructions or a diagnosis other than musculoskeletal tumor; 27 with a tumor-related diagnosis were skeletally immature and underwent distal femoral reconstruction with the intent to perform multiple expansion procedures at a later date, possibly including complete prosthesis exchange; two patients underwent reconstruction with a cementless implant. We previously reported our results of expandable and cementless implants for tumors of the distal femur [16, 17, 36, 64] and did not include them in the current analysis. These exclusions left 186 patients: 98 (53%) males and 88 (47%) females. Their mean age at the time of surgery was 29.0 years (range, 12–79 years). The 186 patients were analyzed overall and according to implant type. We further divided the 186 patients into three subgroups based on disease grade or stage: Group 1 ($n = 43$) were patients with low-grade malignancy (Stage IA or IB), parosteal osteosarcoma, or benign diagnoses; Group 2 ($n = 122$) was comprised of patients with high-grade localized disease (Stage IIA or IIB); and Group 3 ($n = 21$) included patients with Stage III primary

Table 1. Diagnoses

Diagnosis	Number of patients
Group 1 (low grade)	
Giant cell tumor	18 (9.7%)
Parosteal osteosarcoma	14 (7.5%)
Chondrosarcoma (low grade)	7 (3.8%)
Desmoid of bone	3 (1.6%)
Chondroblastoma	1 (0.5%)
Total Group 1	43 (23.1%)
Group 2 (high-grade localized)	
Osteosarcoma (classic high grade)	102 (54.8%)
Chondrosarcoma (high grade)	7 (3.8%)
Malignant fibrous histiocytoma	5 (2.7%)
Ewing's sarcoma	2 (1.1%)
Synovial sarcoma	2 (1.1%)
Malignant giant cell tumor	1 (0.5%)
Leiomyosarcoma	1 (0.5%)
Fibrosarcoma	1 (0.5%)
Alveolar soft parts sarcoma	1 (0.5%)
Total Group 2	122 (65.6%)
Group 3 (Stage III/disseminated)	
Osteosarcoma (Stage III)	11 (5.9%)
Metastatic disease	4 (2.2%)
Malignant fibrous histiocytoma	2 (1.1%)
Fibrosarcoma	2 (1.1%)
Myeloma	1 (0.5%)
Lymphoma	1 (0.5%)
Total Group 3	21 (11.3%)
Total all groups	186 (100.0%)

malignancy of the distal femur, along with patients with metastatic carcinoma to the distal femur, and the single cases of myeloma and lymphoma (Table 1). The latter group was treated as a single cohort owing to similarity in life expectancy among patients with these four diagnoses. At the most recent followup, 65 of the 186 patients had died (35%). The minimum followup was 1 month (mean, 96 months; range, 1–336 months; median, 54.5 months) for all patients and 1 month (mean, 130.4 months; range, 1–336 months) for the 121 surviving patients. Eight patients were lost to followup but were well at the time of the last evaluation (range, 3–13 months). No patients were recalled specifically for this chart review study. We obtained prior approval from our institution's Office for Protection of Research Subjects (UCLA IRB #G08-10-100-01).

From the charts, we recorded the index diagnosis and disease stage at the time of presentation (according to the system described by Enneking et al. [22, 25]), length of followup, postoperative function scores, implant type and manufacturer, and any major postoperative events

(systemic or local complications, repeat surgery for any reason, revision of stemmed components, and/or local recurrence).

All endoprosthetic reconstructions were performed by the same surgeon (JJE), and all tumor resections followed generally accepted oncologic principles [7, 12, 14, 15]. A longitudinal medial incision extended from the tibial tubercle proximally following the course of the sartorius muscle, and the neurovascular bundle was identified and protected. Tourniquets were never used. All previous open biopsy sites were left in continuity with the resected mass; needle biopsy sites were ignored. The femoral and tibial osteotomies were made with the intention that postreconstruction leg lengths would be equal. A rotating-hinge knee mechanism was used in all cases that incorporated an 8-mm all-polyethylene nonmetal-backed tibial component. The distance between the distal end of the metal femoral component and the undersurface of the all-polyethylene tibial component when assembled was 17 mm. To ensure leg length equality, the femoral osteotomy was made 1 cm longer than the femoral component length, and 7 mm of proximal tibia was resected. The location of the patella relative to the joint line was never a conscious consideration. The level of resection was marked on the femur proximally with an osteotome, followed by a slightly more proximal mark on the femur and a mark on the proximal tibia (distal to the level of resection). The distance between the latter two marks was measured and recorded. This preresection distance should equal the postreconstruction distance to ensure limb length equality. A final mark was placed at the most anterior aspect of the femur to ensure proper femoral component rotation as the location of the linea aspera was not always exactly posterior.

After the femoral osteotomy, the proximal marrow was sent for frozen-section analysis to confirm a negative marrow margin. A trial tibial component was placed, and in all cases, an intraoperative radiograph was obtained to ensure placement perpendicular to the mechanical axis of the tibia. The trial hinge mechanism was reduced, and restoration of the preresection extremity length and rotation were verified using marks previously made on the proximal tibia and femur. The neurovascular bundle was palpated to ensure there was not excessive tension on the vessels, and a Doppler probe at the ankle confirmed the presence of the posterior tibial and dorsalis pedis pulses. We routinely used antibiotic-impregnated cement for all endoprosthetic reconstructions. The all-polyethylene tibial and patellar components were cemented first, followed by the femoral component separately. All patients were administered 100 mg Solu-Cortef® (Pfizer Inc, New York, NY) before placement of the femoral component, and the prosthesis was introduced slowly to avoid causing a fat embolism.

Implants were manufactured by one of three companies: Stryker/Howmedica (Mahwah, NJ), Techmedica (Camarillo, CA), and Dow-Corning Wright Corp (Arlington, TN). All implants used a rotating-hinge knee mechanism. The 156 implants (83.9%) manufactured by Stryker/Howmedica used the Kinematic™ rotating-hinge mechanism [33]. The 28 implants (15.1%) manufactured by Techmedica used the Noiles™ rotating hinge, whereas the two (1.1%) manufactured by Dow-Corning Wright used the Lacey rotating-hinge knee (Figs. 1, 2). Initially, the first 101 (54.3%) prostheses were custom designed by two of the senior authors (JMK, JJE) as a one-piece femoral component [56]. Seventy-three of 101 custom implants were Co-Cr-Mo alloy components manufactured by Howmedica. The bodies were casted using

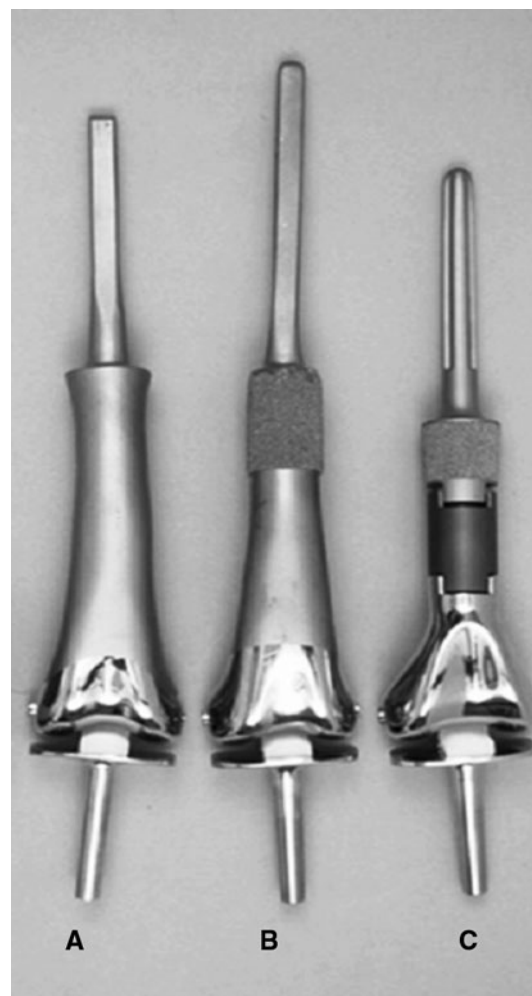
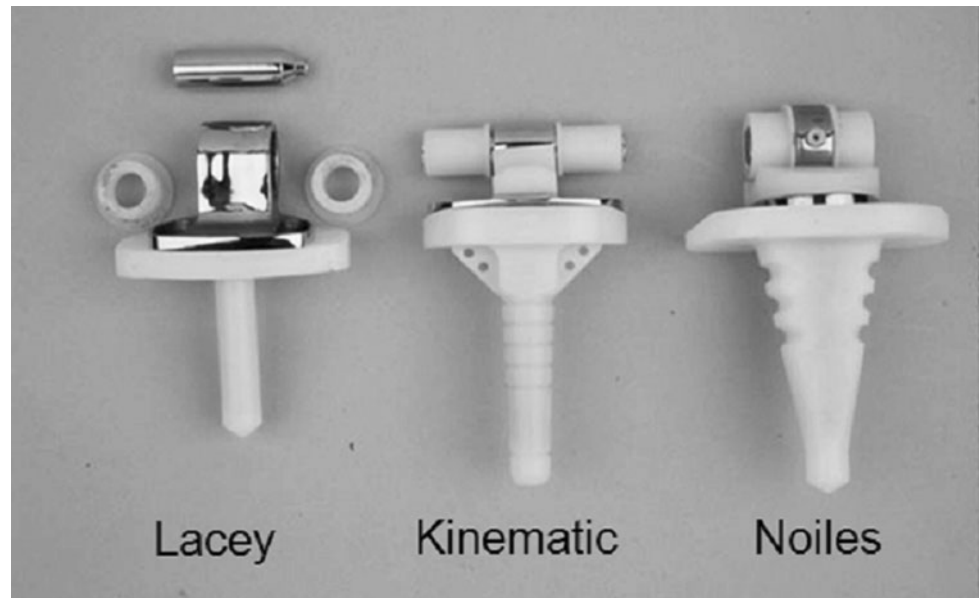


Fig. 1A–C (A) A custom endoprosthesis featuring a body casted by the lost-wax method and used from 1980 to 1985 is shown. The stem, based on the Zickel nail design, was welded to the body. (B) An extramedullary porous coating was added to the prosthesis used from 1985 to 1990, which acts as a scaffolding for soft tissue ingrowth. This presumably protects the stem from debris wear and may reduce aseptic loosening. (C) A contemporary modular endoprosthesis used since 1990 features titanium segments and Co-Cr-Mo alloy Morse tapers that prevent cold welding.

Fig. 2 The Lacey, Kinematic, and Noiles rotating-hinge mechanisms used in this series are shown.



the lost-wax method, and the casted stems, based on the Zickel nail design, were welded to the body. All 28 of the Techmedica components were manufactured completely from titanium. In 1990, modular endoprotheses were introduced and subsequently used in 85 patients (45.7%). Conventional nonmetal-backed polyethylene tibial components were used in all cases. All patellae were resurfaced using a nonmetal-backed all-polyethylene single central-pegged component.

Before the introduction of the continuous passive motion (CPM) machine, patients initially were immobilized in a cast for 2 to 3 weeks before physical therapy. Since the introduction of the CPM machine in the early 1980s, all patients were placed into a CPM machine in the operating room. Motion was commenced from -5° extension to 30° to 45° flexion and gradually increased to greater than 90° flexion before discharge. A towel roll under the heel was used three times daily for 1 hour to ensure full extension was achieved. On the third postoperative day, patients were made weightbearing as tolerated with ambulatory supports and a knee immobilizer, which were used for 6 to 8 weeks. The CPM machine was used at home for 12 hours a day for 1 month to help ensure maximum flexion was achieved.

Patients were followed every 2 to 3 weeks for the first 2 months after surgery, then on a quarterly basis for 2 years, semiannually for an additional 2 years, and annually thereafter. Radiographs of the affected limb were obtained at each postoperative visit, along with quarterly chest radiographs and semiannual chest CT. Postoperative function was evaluated for each patient using the Musculoskeletal Tumor Society (MSTS) function score [23]. One hundred sixty of the 186 patients (86.0%) were available

for functional evaluation and did not undergo amputation during the followup period.

Patient and prosthesis survival rates and 95% confidence intervals (CIs) were determined for all three groups using the Kaplan-Meier product-limit method [34]. Patient survival was analyzed using death attributable to disease progression as an end point. Prosthesis survivorship was determined for custom and modular implants separately using revision of the stemmed components for any reason as an end point. For purposes of implant survival, we did not include surgery attributable to failure of the bushings, the axle, or the metal tibial bearing component, all of which were managed successfully without the need for revision of major stemmed components. Implant and patient survival curves for the two types of implants and three grades or stages of malignancy were compared using the log-rank method [42]. Statistical analysis was performed using a commercially available statistics package (R, Version 2.9.0, The R Foundation for Statistical Computing, Vienna, Austria).

Results

Modular implants had greater survivorship ($p = 0.011$) than those of a custom design, with a 15-year survivorship rate of 93.7% versus 51.7% (Fig. 3). Of the 186 index procedures, 35 stemmed components (18.8%) were revised: 32 revisions were performed owing to mechanical failure, whereas an additional three revisions were necessary owing to nonmechanical complications. Thirty-one custom-casted stems were revised; 19 were revised for aseptic loosening of the femoral stem, nine for fatigue

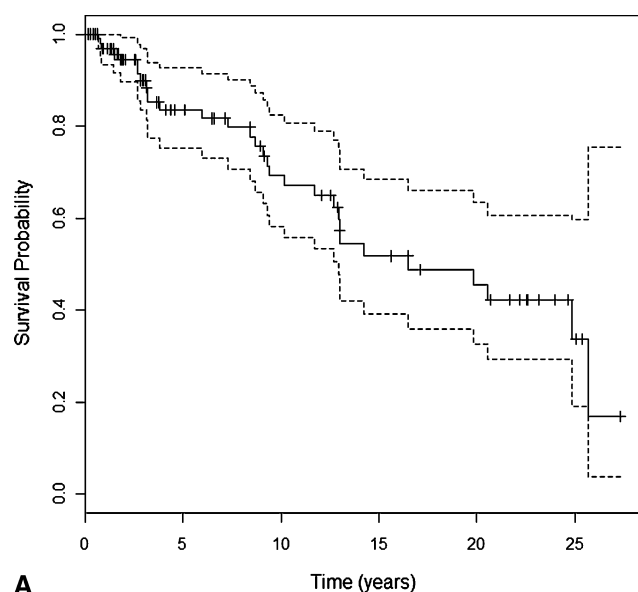
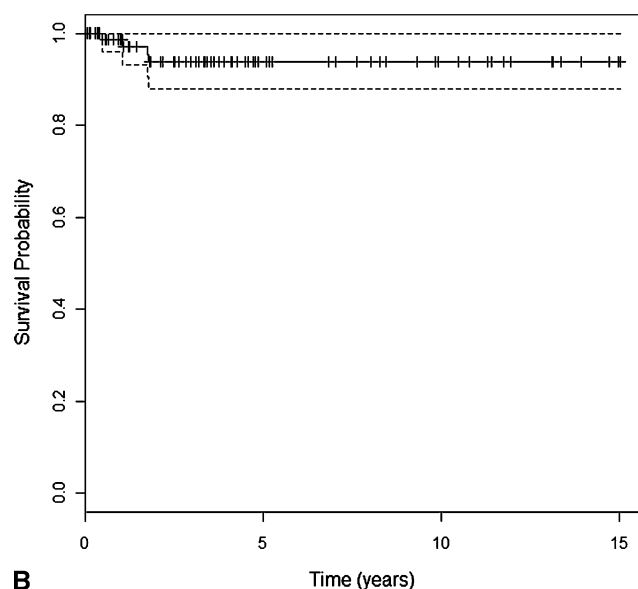
**A****B**

Fig. 3A–B Kaplan-Meier survivorship analyses show (A) custom ($n = 101$) versus (B) modular ($n = 85$) implant survival. The dashed lines represent the 95% CI.

fracture, two for infection, and one for local recurrence. Only four of 85 forged modular components were revised: three for aseptic loosening and one for a fatigue fracture of a casted (not forged) Morse taper component. There were no stem fractures among forged modular implants. Failure of the rotating-hinge mechanism necessitated replacement of the bushings and/or axle without revision of the stemmed components in 22 patients (11.8%) at a mean of 159.7 months (range, 1.6–291.1 months) from the index procedure; six of these patients (3.2%) ultimately required a second bushing change. Using revision of the stemmed components for any reason as an end point, overall

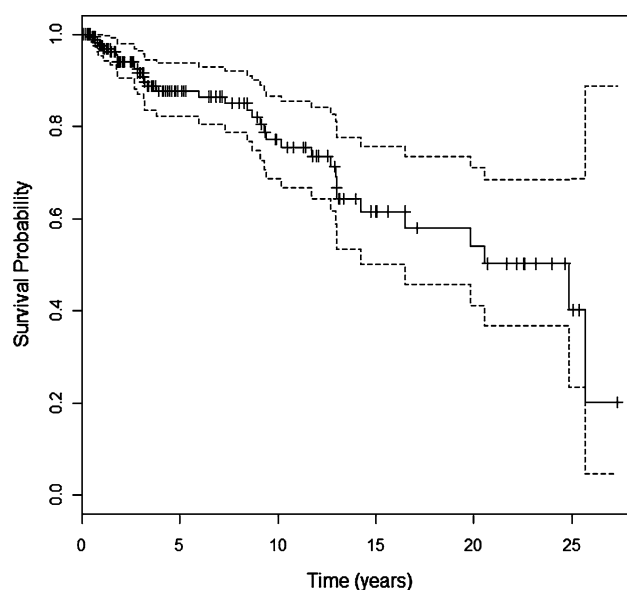


Fig. 4 The Kaplan-Meier survivorship analysis shows overall prosthesis survival ($n = 186$). The dashed lines represent the 95% CI.

prosthesis survival rates at 10, 20, and 25 years were 77.2%, 57.9%, and 50.2%, respectively (Fig. 4; Table 2).

Modular implant survival was greater ($p = 0.001$) than patient survival for those in disease Groups 2 and 3. All patients initially diagnosed with low-grade or aggressive benign tumors (Group 1, $n = 43$) survived (Fig. 5; Table 2). The 10-, 20-, and 25-year disease-specific survival rates for patients diagnosed with high-grade localized disease (Group 2) were 57.7%, 56.0%, and 56.0%, respectively (Fig. 6; Table 2). The 5- and 10-year disease-specific survival rates for patients diagnosed with Stage III sarcomas, metastatic disease, lymphoma, and myeloma (Group 3) were 25.6% and 0%, respectively (Fig. 7; Table 2).

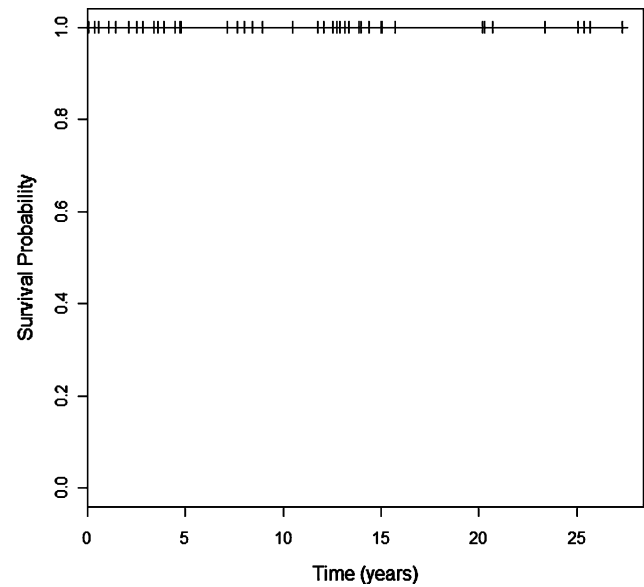
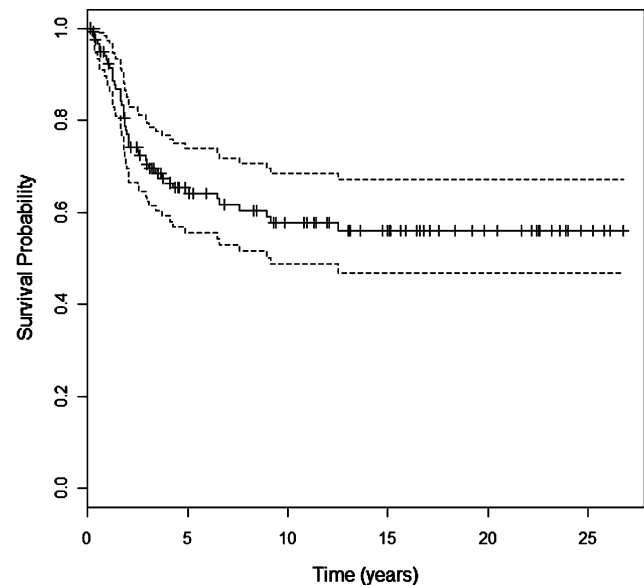
Among the 160 patients for whom we had functional evaluations and who retained their implants, the mean postoperative MSTS score was 86.7% (mean score, 26.0; range, 11–29). The postoperative ROM on final assessment revealed mean flexion of 110.0° (range, 45°–140°), mean passive extension to 1.3° (range, 0°–40°), and mean active extension lag of 6.9° (range, 0°–120°). A postoperative flexion contracture was observed in seven patients, with a mean value of 10.0° (range, 5°–40°).

Seven systemic complications occurred in seven patients, including four cardiac arrhythmias, and single cases of chemotherapy-related fungal sepsis, acute leukemia, and steroid-induced avascular necrosis of multiple joints. One hundred four local complications occurred in 88 patients; a single complication occurred in 72 patients, and 16 patients experienced multiple complications. Complications included mechanical failure in 54 (29.0%; Fig. 8),

Table 2. Implant survival, patient survival, and overall limb salvage data

Survival	5 years			10 years			15 years			20 years			25 years		
	%	95% CI	Upper	%	95% CI	Upper	%	95% CI	Upper	%	95% CI	Upper	%	95% CI	Upper
Implant survival															
Low grade (n = 43)	83.3%	71.9%	96.5%	73.5%	58.5%	92.3%	73.5%	58.5%	92.3%	61.2%	40.1%	93.6%	30.6%	7.2%	100.0%
Stage IIA/IIB (n = 122)	89.8%	83.5%	96.5%	78.4%	68.2%	90.2%	55.7%	41.6%	74.7%	50.7%	35.8%	71.7%	45.0%	29.7%	68.4%
Stage III (n = 21)	85.7%	63.3%	100.0%	NA			NA			NA			NA		
Custom (n = 101)	83.5%	75.2%	92.7%	69.2%	58.1%	82.4%	51.7%	39.1%	68.4%	48.7%	35.9%	66.0%	42.2%	29.4%	60.7%
Modular (n = 85)	93.7%	87.9%	99.9%	93.7%	87.9%	99.9%	93.7%	87.9%	99.9%	NA			NA		
Overall (n = 186)	87.7%	82.2%	93.7%	77.2%	68.7%	86.7%	61.6%	50.1%	75.7%	57.9%	45.6%	73.5%	50.2%	36.8%	68.5%
Patient survival by diagnosis															
Low grade (n = 43)	100.0			100.0			100.0			100.0			100.0		
Stage IIA/IIB (n = 122)	65.3%	56.9%	74.9%	57.7%	48.7%	68.4%	56.0%	46.8%	67.0%	56.0%	46.8%	67.0%	56.0%	46.8%	67.0%
Stage III (n = 21)	25.6%	11.6%	56.4%	NA			NA			NA			NA		
Overall limb salvage	91.3%	86.7%	96.3%	89.0%	83.5%	94.8%	85.2%	77.9%	93.1%	78.8%	68.6%	90.6%	78.8%	68.6%	90.6%

CI = confidence interval; NA = not available.

**Fig. 5** The Kaplan-Meier survivorship analysis shows survival among patients with low-grade or benign disease (Group 1; n = 43).**Fig. 6** The Kaplan-Meier survivorship analysis shows survival among patients with high-grade localized (Stage IIA/IIB) disease (Group 2; n = 122). The dashed lines represent the 95% CI.

superficial wound-related issues in 13 (7.0%), local recurrence in 13 (7.0%), temporary peroneal nerve palsy in seven (3.8%), deep infections in six (3.2%), cement extrusion through a vascular channel in three (1.6%), flexion contracture in three (1.6%), patellofemoral subluxation in two (1.1%), positive oncologic margins in two (1.1%), and stress fracture in one (0.05%). Eighty-one complications required at least one additional surgical procedure. Mechanical failure of the prosthesis occurred in

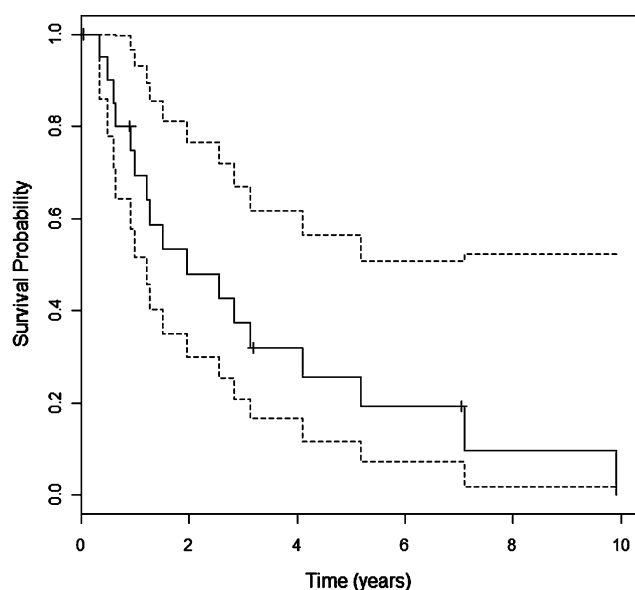


Fig. 7 The Kaplan-Meier survivorship analysis shows patient and prosthesis survival among patients with Stage III primary sarcoma, metastatic disease to the distal femur, myeloma, or lymphoma (Group 3; $n = 21$). The dashed lines represent the 95% CI.

54 cases (29.0%). Thirty-two were stemmed component revisions and 22 involved replacement of the bushings only, as described previously. Six of 13 patients with local recurrence were treated with an amputation, and seven were palliated. Eight of the 13 patients (61.5%) with local recurrence ultimately died of their disease, and five of the 13 (38.5%) are alive. Of the five patients who currently are alive, four remain disease-free at 50, 141, 166, and 205 months. One patient currently is alive with metastatic pulmonary disease at 38 months after the index procedure. Eighteen of the 186 patients (9.7%) ultimately required amputation after either the index or later revision procedure and were categorized as having failed limb salvage efforts. The reason for amputation was infection in nine patients, local recurrence in six, positive surgical margins in two, and metastasis to the pelvis in one.

Discussion

Historically, a debate existed among orthopaedic oncologists regarding which was the most durable method of

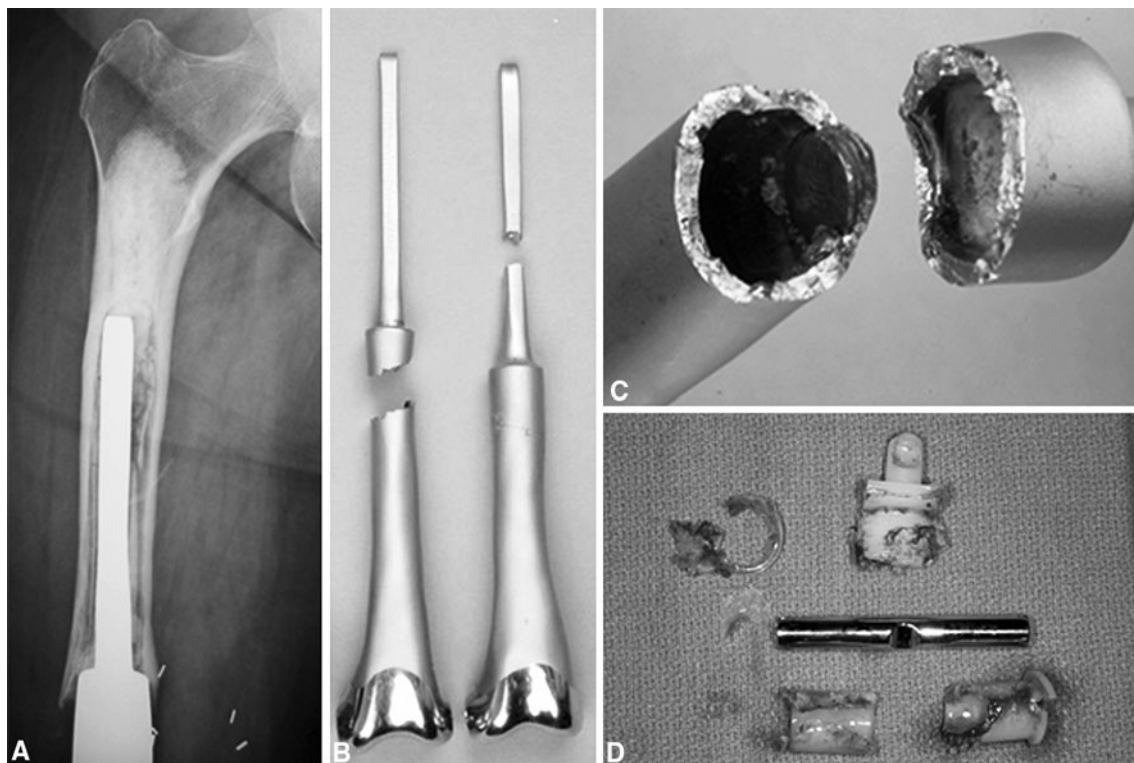


Fig. 8A–D The common modes of mechanical failure seen in this series of cemented rotating-hinge distal femoral endoprostheses from 1980 to 2008 are shown. **(A)** A radiograph shows aseptic loosening of a custom-casted femoral stem 24 years after the index reconstruction. The absence of extramedullary porous coating on the proximal body is evident. In our series, there were 22 total instances of aseptic loosening: 19 custom and three modular. **(B)** Fatigue fractures of a custom-casted femoral stem (right) and femoral body (left) are

illustrated. There was only one fatigue fracture of a modular component, which was a casted (not forged) Morse taper segment. In our series, there were 10 total fatigue fractures: nine custom and one modular. **(C)** An axial photograph shows a fractured hollow, custom-casted femoral body. **(D)** In our series, there were 22 failures of the rotating-hinge bushings, as illustrated in this photograph, 15 custom and seven modular.

reconstruction after distal femoral resection. Although high long-term implant survival and functional scores have been reported with a wide variety of reconstructive methods [5, 7, 14, 44, 53–55, 57, 65], our experience with osteoarticular allografts between 1975 and 1979 was poor, and in 1980 we abandoned this method of reconstruction in favor of a cemented endoprosthetic technique [13, 14, 51]. Recently, critics of this technique have cited high rates of aseptic loosening as the major reason for using alternative fixation methods [2, 38]. Such criticism does not consider the potential improvement in cemented implant survival over historical rates attributable to design modifications. We asked the following four questions: (1) Do newer implant designs perform better than older custom-designed implants? (2) Does tumor diagnosis influence implant survival? (3) What is the typical long-term functional result after distal femoral replacement? (4) What are the complications associated with endoprosthetic reconstruction of the distal femur?

The major limitations of this study are its retrospective design, the lack of a control group, and the lack of a pre-study power analysis. The first two limitations are difficult to overcome for numerous reasons. First, musculoskeletal tumors are rare, and although a prospective design certainly would enhance the validity of our conclusions, it would be exceedingly difficult to amass a large series of patients prospectively. Second, comparison to a control group is virtually impossible because other methods of reconstruction were used only rarely at our institution. In the absence of a prestudy power analysis, we have limited our conclusions to address the differences in survival rates and refrained from drawing conclusions when no difference was seen in the data. The questions addressed at the start of this paper will be addressed in light of these few but important limitations.

Largely owing to the low incidence of musculoskeletal sarcomas, few studies document the long-term durability of contemporary cemented distal femoral endoprostheses (Table 3). Published implant survival rates vary from 46.3% to 93.0%, potentially a reflection of heterogeneous patient and implant study populations. When compared with primary total joint implants, the modifications made to cemented endoprosthetic designs have been relatively few. These modifications include the addition of extramedullary porous coating, the development of modular segments, and the use of forged metals that have the potential to reduce the incidence of fatigue fracture [8, 28, 45, 62]. The evolution of the implants used at our institution reflects this general development of endoprosthetic design (Table 4). The data presented here suggest the use of contemporary modular components improve the durability and longevity of the cemented prosthesis when used in distal femoral applications. Although custom-casted stems can last two to

three decades, modular designs maintain the intrinsic benefit of immediate availability and the ability to intra-operatively tailor components based on the resection level. Malo et al. [44] reported modular implants were associated with an improved MSTs functional score among 56 patients. Numerous authors [8, 43, 48, 70] have similarly reported modular endoprostheses survive longer than historical custom-designed implants. In our series, the mean time to revision of the four failures among modular implants was 12.5 months (range, 1.6–21.4 months), indicating these failures were possibly the result of technical error rather than implant design (Fig. 9). Three of four modular failures were attributable to aseptic loosening, likely the result of poor cement technique as noted previously. The fourth failure of a modular implant was attributable to fatigue fracture of a casted, not forged, Morse taper segment, emphasizing the importance of this particular design feature. The revision implants for the three cases of aseptic loosening have outlasted the original primary reconstructions. Currently, the mean time from revision surgery for these patients is 138.6 months (range, 107.4–181.2 months). All four patients who underwent revision of a modular implant still maintain successful limb salvage. Although an improvement in survival was seen in this series, we recognize the need for novel implant designs in special circumstances, such as short residual periarticular segments, which we have dealt with by designing a custom implant with cross-stem pin fixation [6]. A compressive intramedullary device based on Wolff's law (Compress[®]; Biomet Inc, Warsaw, IN) was developed to improve fixation in such situations and to reduce the need for custom-designed cemented implants. Five- to 10-year reports of implant survivorship after the use of this device have been promising [2, 38].

By stratifying patients according to disease grade and/or stage, we found a comparison of implant to patient survival provides a useful measure of disease-specific implant efficacy (Fig. 10). Patients with low-grade tumors have a normal life expectancy and thus should expect to outlive their prostheses. As a result, this group almost certainly will require at least one revision procedure in their lifetime. However, none of the patients with disseminated, Stage III disease outlived their prosthesis in this series. For patients with high-grade localized disease (Stage IIA/IIB), overall prosthesis survivorship remained greater than patient survival up to a critical time, at which point the rate of prosthetic failure became greater than patient survival. The rate of modular implant survival, however, continued to exceed patient survival with high-grade localized disease to 15 years. As long-term survival of patients with high-grade disease approaches 70% to 80% [39–41, 46, 52, 66, 67], the improved longevity of modular implants seen in this series supports the notion

Table 3. Review of the available literature

Study	Year	Number of patients	Mean followup (years)	Implant survivorship/revision rate ^a			Mean MSTS score ^a	Amputation ^a	Infection ^a	Local recurrence ^a
				0–9 years	10–14 years	15–19 years				
Bradish et al. [4]	1987	40	8	80.0%			15E, 14G, 3F, 5P ^{b,c}	5.0%	7.5%	12.5%
Shih et al. [58]	1993	61	2–6	0–42% ^g			7E, 19G, 15F, 20P ^{b,c}	8.2%	8.2%	4.9%
Capanna et al. [8] ^d	1994	95	4.3	75% ^e			20E, 43G, 12F, 9P ^{b,c}	7.4%	5.0%	5.3%
Rouggraff et al. [54] ^f	1994	34	11		32.4% ^g		76.7% ^h	26.0%	NA	11.0%
Malawer and Chou [43] ⁱ	1995	31	3.5 ^j	80.0%	80.0%		NA ^k	12.9%	19.4%	0.0%
Choong et al. [9]	1996	32	3.5 ^j	6.7% ^g			6E, 14G, 9F, 3P ^{b,c}	0.0%	3.3%	3.1%
Kawai et al. [35]	1998	40	8 ^j	72.0%	58.0%		80.0%	7.5%	10.0%	0.0%
Malo et al. [44] ^l	2001	56	3	NA			80.4%	NA	NA	NA
Bickels et al. [3]	2002	110	7.8 ^j	93.0%	88.0%		94G/E, 9F, 7P ^{b,c}	3.6%	5.4%	5.4%
Zeegen et al. [71] ⁱ	2004	55	5	82% ^m			NA	NA	NA	NA
Torbert et al. [61] ^j	2005	57	4.7	84.0%	66.0%		NA	6.5%	2.2%	6.8%
Frink et al. [26] ⁿ	2005	83	12	86.0%	86.0%	86.0%	88.0%	NA	NA	2.3%
Sharma et al. [57]	2006	77	4.3	84.0%	79.0%		30 ^p	6.5%	7.8%	6.5%
Schwab et al. [55] ^o	2006	43	7.5	NA			78.0%	NA	NA	NA
Gosheger et al. [27] ⁱ	2006	103	3.8	65.9%			80.0%	NA	12.0%	0.5%
Myers et al. [50] ^p	2007	335	12	83.0%	78.0%		NA	17.0%	14.0%	6.0%
Jeys et al. [32] ^{g,i}	2008	228	9 ^j	68.6%	68.6%	46.3%	NA	9.2%	12.7%	5.3%
Current study ^q	2010	186	8	87.7%	77.2%	61.6%	86.7%	9.7%	3.2%	7.0%

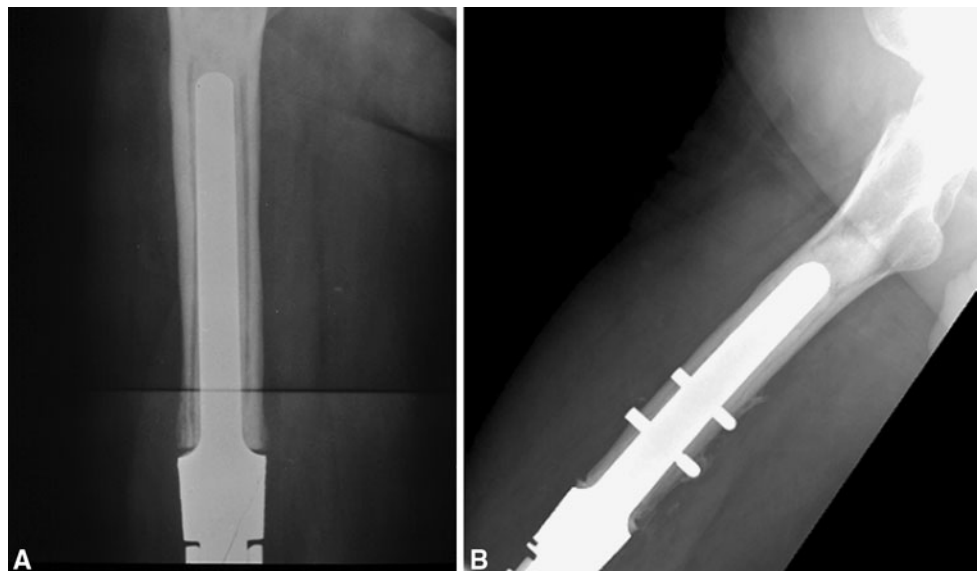
^a Numbers (as reported) converted to percentages for ease of comparison; ^b according to the 1987 scoring system described by Enneking et al. [21]; ^c E = excellent, G = good, F = fair, P = poor, according to the 1987 MSTS scoring system [21]; ^d all uncemented implants; ^e neither revision rates reported nor survivorship analysis done; reported as percentage of good or excellent clinical results; ^f data for all limb salvage reconstructions reported; ^g percentage of implants revised reported; ^h data given for all 73 patients who had limb salvage (including rotationplasties, allograft and allograft-prosthetic composites, and others); ⁱ data for implants at all anatomic sites reported; ^j median; ^k function for all sites reported at 83.3% with no significant difference between anatomic sites; ^l functional outcomes only evaluated; ^m data reported for all 63 implants; ⁿ 83 of 144 patients reported who survived greater than 5 years; ^o only patellofemoral complications reported; ^p includes 162 fixed-hinge knees and 173 rotating-hinge knees; survival of rotating-hinge knees only shown; all prostheses custom-made; ^q Kaplan-Meier survivorship of implant; MSTS = Musculoskeletal Tumor Society; NA = not available or not studied.

Table 4. Distal femoral implant evolution at University of California Los Angeles*

Date	Implant design	Manufacturer/features	Tumor group (n = 186)
1980–1990	Custom (JJE/JMK)	Stryker/Howmedica	73
		Kinematic™ rotating hinge	
		Made of vitallium	
		Casted hollow body by lost-wax method	
		Welded Zickel nail stem	
1990–2003	Modular	Extramedullary porous coating added in 1985 [61]	28
		Techmedica	
		All-titanium one piece	
		Noiles™ hinge	
		Total custom implants	
1990–2003	Modular	Stryker/Howmedica	53
		Kinematic™ rotating hinge	
		Forged modular replacement system	
		Titanium segments	
		Extramedullary porous coating	
2003–2008	Modular	Dow-Corning Wright	2
		Modular titanium	
		Lacey hinge	
		Stryker Global Modular Replacement System	
		Kinematic™ rotating hinge	
2003–2008	Modular	Forged modular components	30
		Titanium segments	
		Extramedullary porous coating	
		Larger axle and bushings	
		Press-fit stem option (none in this series)	
2003–2008	Modular	Cobalt-chrome Morse taper	85
		Total modular implants	

* All components in this series were cemented; all tibial components were nonmetal-backed, all-polyethylene; all used a rotating-hinge knee mechanism; all patellar components were all-polyethylene, nonmetal-backed, with a single central peg.

Fig. 9A–B (A) An AP radiograph of the femur shows aseptic loosening of the femoral stem 12 months after endoprosthetic reconstruction with a contemporary modular implant. We suspect this occurred owing to last-minute rotational adjustment of the stem as the cement was curing. (B) A lateral radiograph shows the femur 12 years after revision to a larger cemented stem and in this case with cross-stem pin fixation, which is our preferred method of reconstruction for the majority of failures attributable to aseptic loosening.



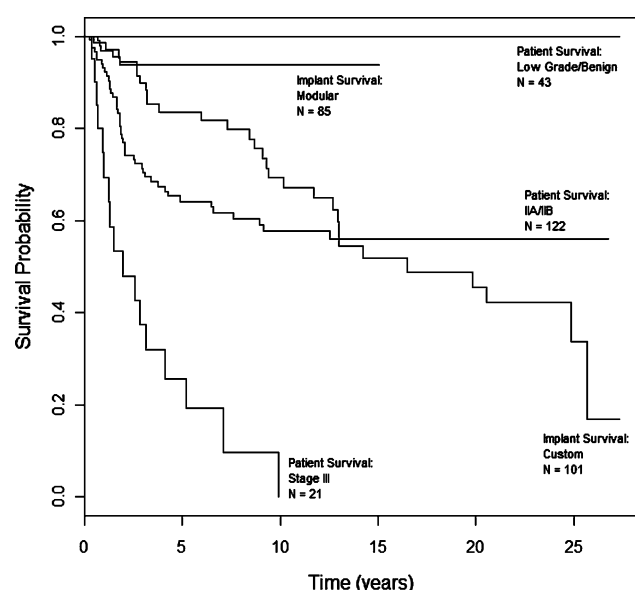


Fig. 10 A graph shows implant versus patient survival for the entire study cohort. Modular implants performed better than custom implants, with 15-year survival rates of 93.7% versus 51.7%, respectively. Patients with low-grade or benign disease and long-term survivors with high-grade localized disease should expect to undergo at least one revision procedure in their lifetime.

that a cemented endoprosthesis will continue to provide a durable method of reconstruction.

The functional scores were high for the majority of patients who underwent endoprosthetic distal femoral reconstructions (Table 3). Functional scores are assigned subjectively, and although newer scoring systems have attempted to eliminate subjective terminology, a precise and accurate measurement of function remains elusive. Despite these limitations, however, our results confirm the findings of previous studies, that favorable long-term function is possible after cemented distal femoral endoprosthetic reconstructions.

The most common local complications in our patients included mechanical failure, tumor recurrence, and infection. All 54 cases of mechanical failure (including modular and custom implants) were salvaged with revision to a larger stem, cross-stem fixation, or new components. Similar to findings described elsewhere, mechanical failures of this nature did not seem to compromise the overall limb salvage effort [59, 68]. Infection, however, worsened the prognosis. Five of 19 patients with wound-related complications that occurred after the index procedure required an amputation, and among an additional six patients who had a deep infection after a second or third procedure, four required an amputation. The total amputation rate in this series for all wound-related complications after either the index or revision procedure was nine of 25 (36.0%). We previously reported our preferred method of

carrying for patients with wound-related issues after endoprosthetic replacement [18]. Local recurrence portended a poor prognosis in this series as 61.5% of patients had died by the time of the most recent followup.

Our study reports the improved survival of cemented distal femoral endoprostheses during the past three decades. Contemporary modular forged implants performed better than the custom-designed prostheses of the 1970s and 1980s. Although failures may occur, mechanical complications can be revised and potentially outlast the original reconstruction. We recognize revision procedures will be necessary for patients with long-term life expectancy, and the need for continued improvement in reconstruction techniques and implant design, as high-grade disease-specific survival rates may continue to improve.

Acknowledgments We thank Brigid Brett-Esborn for assistance with preparation of this manuscript.

Open Access This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

References

- Bacci G, Briccoli A, Longhi A, Ferrari S, Mercuri M, Faggioli F, Versari M, Picci P. Treatment and outcome of recurrent osteosarcoma: experience at Rizzoli in 235 patients initially treated with neoadjuvant chemotherapy. *Acta Oncol.* 2005;44:748–755.
- Bhangu AA, Kramer MJ, Grimer RJ, O'Donnell RJ. Early distal femoral endoprosthetic survival: cemented stems versus the Compress implant. *Int Orthop.* 2006;30:465–472.
- Bickels J, Wittig JC, Kollender Y, Henshaw RM, Kellar-Graney KL, Meller I, Malawer MM. Distal femur resection with endoprosthetic reconstruction: a long-term followup study. *Clin Orthop Relat Res.* 2002;400:225–235.
- Bradish CF, Kemp HB, Scales JT, Wilson JN. Distal femoral replacement by custom-made prostheses: clinical follow-up and survivorship analysis. *J Bone Joint Surg Br.* 1987;69:276–284.
- Brigman BE, Hornicek FJ, Gebhardt MC, Mankin HJ. Allografts about the knee in young patients with high-grade sarcoma. *Clin Orthop Relat Res.* 2004;421:232–239.
- Cannon CP, Eckardt JJ, Kabo JM, Ward WG Sr, Kelly CM, Wirganowicz PZ, Asavamongkolkul A, Nieves R, Eilber FR. Custom cross-pin fixation of 32 tumor endoprostheses stems. *Clin Orthop Relat Res.* 2003;417:285–292.
- Cannon CP, Zeegen E, Eckardt JJ. Techniques in endoprosthetic reconstruction. *Oper Tech Orthop.* 2005;14:225–235.
- Capanna R, Morris HG, Campanacci D, Del Ben M, Campanacci M. Modular uncemented prosthetic reconstruction after resection of tumours of the distal femur. *J Bone Joint Surg Br.* 1994;76: 178–186.
- Choong PF, Sim FH, Pritchard DJ, Rock MG, Chao EY. Mega-prostheses after resection of distal femoral tumors: a rotating hinge design in 30 patients followed for 2–7 years. *Acta Orthop Scand.* 1996;67:345–351.
- Dahlin DC. *Bone Tumors: General Aspects and Data on 6221 Cases.* Springfield, IL: Charles C. Thomas; 1978:226–273.

11. Damron TA, Ward WG, Stewart A. Osteosarcoma, chondrosarcoma, and Ewing's sarcoma: National Cancer Data Base Report. *Clin Orthop Relat Res.* 2007;459:40–47.
12. Eckardt JJ, Eilber FR. Endoprosthetic replacement. *Curr Orthop.* 1993;7:148–156.
13. Eckardt JJ, Eilber FR, Dorey FJ, Mirra JM. The UCLA experience in limb salvage surgery for malignant tumors. *Orthopedics.* 1985;8:612–621.
14. Eckardt JJ, Eilber FR, Grant TO, Mirra JM, Weisenberger TH, Dorey FJ. Management of Stage IIB osteogenic sarcoma: experience at the University of California, Los Angeles. *Cancer Treatment Symposia. Volume 3: National Institutes of Health Consensus Development Conference on Limb Sparing Treatment of Adult Soft Tissue Sarcomas and Osteosarcomas.* Washington, DC: National Institutes of Health; 1985:117–130.
15. Eckardt JJ, Eilber FR, Rosen G, Mirra JM, Dorey FJ, Ward WG, Kabo JM. Endoprosthetic replacement for Stage IIB Osteosarcoma: the UCLA Experience 1980–1988. *Clin Orthop Relat Res.* 1991;270:202–213.
16. Eckardt JJ, Kabo JM, Kelley CM, Ward WG Sr, Asavamongkolkul A, Wirganowicz PZ, Yang RS, Eilber FR. Expandable endoprosthesis reconstruction in skeletally immature patients with tumors. *Clin Orthop Relat Res.* 2000;373:51–61.
17. Eckardt JJ, Kabo JM, Kelly CM, Ward WG Sr, Cannon CP. Endoprosthetic reconstructions for bone metastases. *Clin Orthop Relat Res.* 2003;415(suppl):S254–S262.
18. Eckardt JJ, Lesavoy MA, Debow TJ, Wachym PA. Exposed endoprosthesis: management protocol using muscle and myocutaneous flap coverage. *Clin Orthop Relat Res.* 1990;251:220–229.
19. Eilber FR, Eckardt J, Morton DL. Advances in the treatment of sarcomas of the extremity: current status of limb salvage. *Cancer.* 1984;54(11 suppl):2695–2701.
20. Eilber FR, Mirra J, Eckardt J, Kern D. Intra-arterial adriamycin, radiation therapy, and surgical excision for extremity skeletal and soft tissue sarcomas. *Dev Oncol.* 1984;26:141–154.
21. Enneking W. Modification of the system for functional evaluation in the surgical management of musculoskeletal tumors. *Limb Salvage in Musculoskeletal Oncology.* New York: Churchill-Livingston; 1987:626–639.
22. Enneking WF. Staging of musculoskeletal tumors. In: Enneking WF, ed. *Musculoskeletal Tumor Surgery.* Vol 1. New York, NY: Churchill Livingstone; 1983:87–88.
23. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res.* 1993;286:241–246.
24. Enneking WF, Shirley PD. Resection-arthrodesis for malignant and potentially malignant lesions about the knee using an intramedullary rod and local bone grafts. *J Bone Joint Surg Am.* 1977;59:223–236.
25. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin Orthop Relat Res.* 1980;153:106–120.
26. Frink SJ, Rutledge J, Lewis VO, Lin PP, Yasko AW. Favorable long-term results of prosthetic arthroplasty of the knee for distal femur neoplasms. *Clin Orthop Relat Res.* 2005;438:65–70.
27. Gosheger G, Gebert C, Ahrens H, Streithuenger A, Winkelmann W, Harges J. Endoprosthetic reconstruction in 250 patients with sarcoma. *Clin Orthop Relat Res.* 2006;450:164–171.
28. Henshaw R, Malawar M. Review of endoprosthetic reconstruction in limb-sparing surgery. In: Malawar MM, Sugarbaker PH, eds. *Musculoskeletal Cancer Surgery: Treatment of Sarcomas and Allied Diseases.* Norwell, MA: Kluwer Academic Publishers; 2001:383–404.
29. Horowitz SM, Glasser DB, Lane JM, Healey JH. Prosthetic and extremity survivorship after limb salvage for sarcoma: how long do the reconstructions last? *Clin Orthop Relat Res.* 1993;293:280–286.
30. Hua J, Walker PS. A comparison of cortical strain after cemented and press-fit proximal and distal femoral replacement. *J Orthop Res.* 1992;10:739–744.
31. Huvo AG. Bone tumors: malignant—osteogenic sarcoma. *Bone Tumor: Diagnosis, Treatment and Prognosis.* Philadelphia, PA: WB Saunders; 1979:85–155.
32. Jeys LM, Kulkarni A, Grimer RJ, Carter SR, Tillman RM, Abudu A. Endoprosthetic reconstruction for the treatment of musculoskeletal tumors of the appendicular skeleton and pelvis. *J Bone Joint Surg Am.* 2008;90:1265–1271.
33. Kabo JM, Yang RS, Dorey FJ, Eckardt JJ. In vivo rotational stability in the kinematic rotating-hinge knee. *Clin Orthop Relat Res.* 1997;336:166–176.
34. Kaplan EL, Meier P. Nonparametric estimation from incomplete observation. *J Am Stat Assoc.* 1958;53:457–481.
35. Kawai A, Muschler GF, Lane JM, Otis JC, Healey JH. Prosthetic knee replacement after resection of a malignant tumor of the distal part of the femur: medium to long-term results. *J Bone Joint Surg Am.* 1998;80:636–647.
36. Kay RM, Kabo JM, Seeger LL, Eckardt JJ. Hydroxyapatite-coated distal femoral replacements: preliminary results. *Clin Orthop Relat Res.* 1994;302:92–100.
37. Kotz R, Salzer M. Rotation-plasty for childhood osteosarcoma of the distal part of the femur. *J Bone Joint Surg Am.* 1982;64:959–969.
38. Kramer MJ, Tanner BJ, Horvai AE, O'Donnell RJ. Compressive osseointegration promotes viable bone at the endoprosthetic interface: retrieval study of Compress implants. *Int Orthop.* 2008;32:567–571.
39. Lewis IJ, Nooij MA, Whelan J, Sydes MR, Grimer R, Hogendoorn PC, Memon MA, Weeden S, Uscinska BM, van Glabbeke M, Kirkpatrick A, Hauben EI, Craft AW, Taminiu AH; MRC BO06 and EORTC 80931 collaborators; European Osteosarcoma Intergroup. Improvement in histologic response but not survival in osteosarcoma patients treated with intensified chemotherapy: a randomized phase III trial of the European Osteosarcoma Intergroup. *J Natl Cancer Inst.* 2007;99:112–128.
40. Link MP, Goorin AM, Horowitz M, Meyer WH, Belasco J, Baker A, Ayala A, Shuster J. Adjuvant chemotherapy of high-grade osteosarcoma of the extremity: updated results of the Multi-Institutional Osteosarcoma Study. *Clin Orthop Relat Res.* 1991;270:8–14.
41. Link MP, Goorin AM, Miser AW, Green AA, Pratt CB, Belasco JB, Pritchard J, Malpas JS, Baker AR, Kirkpatrick JA, et al. The effect of adjuvant chemotherapy on relapse-free survival in patients with osteosarcoma of the extremity. *N Engl J Med.* 1986;314:1600–1606.
42. Machin D, Palmer MKB. Comparison of 2 survival curves. In: Machin D, Palmer MKB, eds. *Survival Analysis: A Practical Approach.* Chichester, UK: Bookcraft; 1995:66–75.
43. Malawar MM, Chou LB. Prosthetic survival and clinical results with use of large-segment replacements in the treatment of high-grade bone sarcomas. *J Bone Joint Surg Am.* 1995;77:1154–1165.
44. Malo M, Davis AM, Wunder J, Masri BA, Bell RS, Isler MH, Turcotte RE. Functional evaluation in distal femoral endoprosthetic replacement for bone sarcoma. *Clin Orthop Relat Res.* 2001;389:173–180.
45. Marcove RC, Lewis MM, Rosen G, Huvo AG. Total femur and total knee replacement: a preliminary report. *Clin Orthop Relat Res.* 1977;126:147–152.
46. Marina N, Gebhardt M, Teot L, Gorlick R. Biology and therapeutic advances for pediatric osteosarcoma. *Oncologist.* 2004;9:422–441.
47. Mirra JM. High grade malignant intraosseous lesions associated with 'reactive' osteoid and woven-bone production. *Bone*

- Tumors: Diagnosis and Treatment*. Philadelphia, PA: JB Lippincott; 1980:138–161.
48. Mittermayer F, Windhager R, Dominkus M, Krepler P, Schwameis E, Sluga M, Kotz R, Strasser G. Revision of the Kotz type of tumour endoprosthesis for the lower limb. *J Bone Joint Surg Br*. 2002;84:401–406.
 49. Muscolo DL, Ayerza MA, Aponte-Tinao LA, Ranalletta M. Use of distal femoral osteoarticular allografts in limb salvage surgery. *J Bone Joint Surg Am*. 2005;87:2449–2455.
 50. Myers GJ, Abudu AT, Carter SR, Tillman RM, Grimer RJ. Endoprosthetic replacement of the distal femur for bone tumours: long-term results. *J Bone Joint Surg Br*. 2007;89:521–526.
 51. National Institutes of Health. Limb-sparing treatment of adult soft-tissue sarcomas and osteosarcomas. National Institutes of Health Consensus Development Conference Statement. *Natl Inst Health Consens Dev Conf Consens Statement*. 1985;5:18.
 52. Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR, eds. *Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975–1995*. NIH Publication Number 99–4649. Bethesda, MD: National Institutes of Health; 1999.
 53. Roberts P, Chan D, Grimer RJ, Sneath RS, Scales JT. Prosthetic replacement of the distal femur for primary bone tumours. *J Bone Joint Surg Br*. 1991;73:762–769.
 54. Rougraff BT, Simon MA, Kneisl JS, Greenberg DB, Mankin HJ. Limb salvage compared with amputation for osteosarcoma of the distal end of the femur: a long-term oncological, functional, and quality-of-life study. *J Bone Joint Surg Am*. 1994;76:649–656.
 55. Schwab JH, Agarwal P, Boland PJ, Kennedy JG, Healey JH. Patellar complications following distal femoral replacement after bone tumor resection. *J Bone Joint Surg Am*. 2006;88:2225–2230.
 56. Seeger LL, Farooki S, Yao L, Kabo JM, Eckardt JJ. Custom endoprostheses for limb salvage: a historical perspective and imaging evaluation. *AJR Am J Roentgenol*. 1998;171:1525–1529.
 57. Sharma S, Turcotte RE, Isler MH, Wong C. Cemented rotating-hinge endoprosthesis for limb salvage of distal femur tumors. *Clin Orthop Relat Res*. 2006;450:28–32.
 58. Shih LY, Sim FH, Pritchard DJ, Rock MG, Chao EY. Segmental total knee arthroplasty after distal femoral resection for tumor. *Clin Orthop Relat Res*. 1993;292:269–281.
 59. Shin DS, Weber KL, Chao EY, An KN, Sim FH. Reoperation for failed prosthetic replacement used for limb salvage. *Clin Orthop Relat Res*. 1999;358:53–63.
 60. Simon MA, Aschliman MA, Thomas N, Mankin HJ. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. *J Bone Joint Surg Am*. 1986;68:1331–1337.
 61. Torbert JT, Fox EJ, Hosalkar HS, Ogilvie CM, Lackman RD. Endoprosthetic reconstructions: results of long-term followup of 139 patients. *Clin Orthop Relat Res*. 2005;438:51–59.
 62. Ward WG, Johnston KS, Dorey FJ, Eckardt JJ. Extramedullary porous coating to prevent diaphyseal osteolysis and radiolucent lines around proximal tibial replacements: a preliminary report. *J Bone Joint Surg Am*. 1993;75:976–987.
 63. Ward WG, Johnston KS, Dorey FJ, Eckardt JJ. Loosening of massive femoral cemented endoprostheses: radiographic evidence of loosening mechanism. *J Arthroplasty*. 1997;12:741–750.
 64. Ward WG, Yang R-S, Eckardt JJ. Endoprosthetic bone reconstruction following malignant tumor resection in skeletally immature patients. *Orthop Clin North Am*. 1996;27:493–502.
 65. Weis LD. The success of limb-salvage surgery in the adolescent patient with osteogenic sarcoma. *Adolesc Med*. 1999;10:451–458, xii.
 66. Wilkins RM, Cullen JW, Camozzi AB, Jamroz BA, Odom L. Improved survival in primary nonmetastatic pediatric osteosarcoma of the extremity. *Clin Orthop Relat Res*. 2005;438:128–136.
 67. Wilkins RM, Cullen JW, Odom L, Jamroz BA, Cullen PM, Fink K, Peck SD, Stevens SL, Kelly CM, Camozzi AB. Superior survival in treatment of primary nonmetastatic pediatric osteosarcoma of the extremity. *Ann Surg Oncol*. 2003;10:498–507.
 68. Wilkins RM, Kelly CM. Revision of the failed distal femoral replacement to allograft prosthetic composite. *Clin Orthop Relat Res*. 2002;397:114–118.
 69. Winkler K, Beron G, Kotz R, Salzer-Kuntschik M, Beck J, Beck W, Brandeis W, Ebell W, Erttmann R, Göbel U, et al. Neoadjuvant chemotherapy for osteogenic sarcoma: results of a Cooperative German/Austrian study. *J Clin Oncol*. 1984;2:617–624.
 70. Wu CC, Henshaw RM, Pritsch T, Squires MH, Malawer MM. Implant design and resection length affect cemented endoprosthesis survival in proximal tibial reconstruction. *J Arthroplasty*. 2008;23:886–893.
 71. Zeegen EN, Aponte-Tinao LA, Hornicek FJ, Gebhardt MC, Mankin HJ. Survivorship analysis of 141 modular metallic endoprostheses at early followup. *Clin Orthop Relat Res*. 2004;420:239–250.